Larval Therapy: A Novel Treatment in Eliminating Methicillin-Resistant *Staphylococcus aureus* From Diabetic Foot Ulcers

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Overuse of antibiotics and the selection of broad- rather than narrow-spectrum agents have contributed to the high prevalence of methicillin-resistant *Staphylococcus aureus* (MRSA) colonization in diabetic foot wounds. Consequently, MRSA is now an endemic in both the community and hospital environments (1,2). We previously highlighted the problem (3) of MRSA colonization in our diabetic foot clinic (40% of *S. aureus* isolates were MRSA). A follow-up study (4) demonstrated that the number of foot wounds from which MRSA was isolated doubled in a 3-year period. Although terms such as critical colonization are not clearly defined, the risk of MRSA infection and bacteremia in patients with colonized ulcers is recognized (5,6). Furthermore, there is evidence (4) that MRSA colonization of chronic ulcers is associated with delayed healing times. Strategies to eliminate MRSA from colonized wounds are therefore essential and should include the use of simple, low-cost, effective treatments.

Larval therapy is suggested (7) to successfully remove sloughy necrotic tissue from ulcers and to facilitate healing. We hypothesized that larval therapy would eradicate MRSA colonization from diabetic foot ulcers. Here, we report the results of our preliminary observational study.

RESEARCH DESIGN AND METHODS

— Consecutive patients aged 18–80 years with MRSA-colonized chronic diabetic foot ulcers for >3 weeks duration were included in the study. Subjects on antibiotic treatment specific for MRSA (vancomycin or linezolid), on anticoagulation therapy, or requiring immediate systemic antimicrobial treatment or urgent surgical management were excluded. All patients were assessed by the neuropathy disability score and vibration perception threshold (VPT) (9). Ischemia was defined as nonpalpable pedal pulses and ankle-branchial systolic blood pressure index. An ulcer was deemed to be neuropathic if VPT was >25 V, and/or neuropathy disability score was >3, and neuroischemic if VPT was >25 V with absent foot pulses/ankle-branchial systolic blood pressure index <0.7. MRSA colonization was defined as the isolation of MRSA from the ulcer in subjects without clinical and/or laboratory signs of systemic infection. MRSA status was evaluated by semiquantitative wound tissue cultures taken from the wound base after debridement at baseline and before each larval application.

Sterile free-range larvae of the green bottle fly *Lucilia Sericata* were applied to the MRSA-colonized ulcers for 4 days at densities determined as ~10 larvae/cm^2 (7). The primary end point was complete eradication of MRSA from the ulcer following a minimum of two and a maximum of eight larval applications per ulcer. Patients with MRSA-positive wound cultures were all screened for MRSA carriage at other sites (nose, perineum, or both) in accordance with the hospital MRSA screening policy. A 5-day self-treatment regime for MRSA eradication was followed in those patients with positive MRSA body screening with the use of Mupirocin nasal ointment, Aquacept body wash, and Aquacept shampoo. Ulcer size was measured with the digital planimetry system (Visitrak) (10) by the same clinician after debridement. Appropriate pressure-relieving dressings (e.g., Allevyn pads) were used to prevent damage of the larvae during treatment, in addition to off-loading modalities (DH Walker; Ossur, Aliso Viejo, CA). No topical antimicrobial agents or growth factors were used on the study ulcer.

RESULTS

— In the study, 13 consecutive diabetic patients with MRSA-colonized ulcers were included (Table 1), >60% of whom had a past history of ulcers. The study ulcers were chronic (average duration 3 months), of neuroischemic etiology (87%), and were located distal to the malleoli. None of the isolated MRSA strains were multiresistant or vancomycin resistant. MRSA colonization was related to hospitalization (61%), antibiotic treatment that was current (31%) rather than prolonged (15%), and residency in a nursing home (8%). MRSA colonization was eliminated from all but 1 of the 13 ulcers (92%) after a mean of three applications with a mean duration of 19 days (range 7–45). During the treatment period, no adverse events were recorded. There was a reduction in sloughy necrotic tissue and an increase of granulation tissue on removal of the last larval application.

The mean duration of larval therapy was 3 weeks, which is far shorter than the 28-week (range 3–60) duration for the conventional treatment for MRSA decontamination in diabetic foot ulcers (4). The

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Abbreviations: MRSA, methicillin-resistant *Staphylococcus aureus*; VPT, vibration perception threshold.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

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Table 1—*Descriptive statistics of the study population and foot ulcers pre- and post-larval treatment*

Sex (male)	10 (77)
Age (years)	62.6 ± 11.4 (46–79)
BMI (kg/m^2)	25.7 ± 4.5 (18.5–37.0)
Type 2 diabetes	8 of 13 (61)
Diabetes duration (years)	23.2 ± 16.7 (2–51)
Neuroischaemic:neuropathic ulcers	13:2 (87:13)
Forefoot:midfoot:hindfoot	10:2:3 (67:13:20)
Ulcer duration (weeks)	12.5 ± 11.4 (3–38)
Number of applications per ulcer	3.1 ± 1.6 (2–7)
Number of pots applied per ulcer	1.7 ± 1.7 (0.5–7.0)
Larva Rx total duration (days)	18.8 ± 12.8 (7–45)
Initial size (cm^2)	3.14 ± 3.15 (0.4–11.1)
Final size (cm^2)	2.39 ± 2.21 (0.2–8.0)
MRSA elimination from ulcer at disharge	12 of 13 (92)
MRSA body screening + pre-larval Rx	11 of 13 (85)
MRSA body screening + at discharge	7 of 13 (54)

Data are mean ± SD (range) or ratio (%) unless otherwise indicated. Rx, prescription.

mean wound area was smaller at discharge from the study, but the reduction in size was not significant compared with the baseline, probably due to the short duration of larval treatment.

CONCLUSIONS — We have demonstrated for the first time, in this preliminary study, the potential of larval therapy to eliminate MRSA colonization of diabetic foot ulcers. Although ours was an observational study, the high success rate of larval treatment in eradicating MRSA colonization from diabetic foot ulcers is promising. If confirmed in a future randomized trial, larval treatment would offer the first noninvasive and risk-free treatment of this increasing problem. There were no complaints reported during larval therapy regarding pain or tenderness around the ulcer. The advantages of larvae on eradication of MRSA colonization and the absence of systemic side effects make the larvae a safe and cost-effective treatment in contrast to expensive and potentially toxic antibiotic therapies, such as vancomycin. The efficacy and superiority of larval therapy in eradicating MRSA colonization compared with conventional treatment needs to be further investigated in larger randomized controlled trials.

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